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EXAMINER
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ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary

Application No.	Applicant(s)
09/763,293	LIDER et al
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 25, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12, 14, and 18* is/are pending in the application.

4a) Of the above, claim(s) *5, 6, 9, and 10* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 7, 8, 11, 12, 14, and 18* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3, 8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election

1a. Applicant's election of peptide 2 (PEP2, SEQ ID NO:1), in Paper No.10, filed on 07 October 2002 is acknowledged. Claims 1-4, 7-8 and 18 read on the elected species. Applicants' understanding that upon allowance of a generic claim, claims to additional species which are written in dependent form or otherwise include all of the limitations of an allowed generic claim will also be considered, is accurate.

1b. Applicant is thanked for using sequence identifiers for the claimed peptides, when appropriate.

1c. Claims 13, 15-17 have been canceled in the preliminary amendment filed on 21 February 2001. Claims 5, 6, 9-10 are withdrawn from consideration by the Examiner as they are drawn to non-elected species. Claims 4 and 8 will be examined in so far as they pertain to pep2 (i.e SEQ ID NO:1). Thus claims 1-4, 7-8, 11-12, 14 and 18 are under consideration.

Claim objections

2. Claims 4, 8 are objected to because of the following informalities:

2a. Claims 4 and 8 recite non-elected species.

2b. Claims 4 and 7 are objected to because of the following informalities:

Claims 4 and 7 recite both the actual amino acid sequences and the SEQ ID Nos for the claimed peptides. The recitation of the actual amino acid sequences and the SEQ ID Nos in the claims is redundant and renders the claims unclear. It is suggested that the recitation of the actual

amino acid sequences be deleted and the peptides be identified only with the appropriate SEQ ID Nos.

Appropriate correction is required.

3. The preliminary amendment filed on 21 February 2001, has been entered in part. Claims 13 and 15-17 have been canceled. However, claims 3, 4, 14 and 18 have not been amended, because the preliminary amendment amending these claims is improper. The desired changes must be shown by brackets (for deleted matter) or underlying (for added matter), (37 CFR §1.21)

Claim rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 4, 7-8, 11-12, 14 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a synthetic peptide, said peptide consisting of the amino acid sequence set forth in SEQ ID NO:1, (i.e pep2), said peptide having in vitro inhibitory effects on the following: (I) adhesion of activated T cells to fibronectin, laminin and collagen-type IV, (ii) chemotactic migration of T cells through fibronectin; (iii) and spontaneous or TNF-α induced secretion of IL-8 or IL-1 β from intestinal epithelial cells, does not reasonably provide enablement for "all' possible IL-2 derived synthetic peptides having inhibitory effects on the in vitro processes recited in claim 2, or "all" possible peptides that are obtained by replacement, addition or deletion of one or more natural or non-natural amino acid residues of peptide of SEQ ID NO:1, or chemical derivatives or cyclic derivatives or dual peptides of pep2, or multimers of said peptides, nor is instant

specification enabling for IL-2 derived peptides obtained by any of the limitations recited in claim 7 sub-parts a to m. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is interpreted as being drawn to a synthetic peptide derived from IL-2, which has an anti-inflammatory effect. Claims 1 and 2 are drawn to "all" possible synthetic IL-2 derived peptides having anti-inflammatory effects, which also inhibit the processes recites in claim 2. However, instant specification is only enabling for the peptide consisting the amino acid sequence set forth in SEQ ID NO:1, said peptide derived from IL-2, said peptide having the specific activities recited in claim 3. Instant specification discloses that pep2 (SEQ ID NO:1) ,which is amino acid residues 136-143 of IL-2, (page 6, line 16), displays inhibitory effects on IL-2 induced adhesion of T cells to fibronectin, collagen IV or laminin, inhibits T cell chemotactic migration induced by IL-2 or MIP-1β, and inhibits spontaneous or TNF-α induced IL-8 or IL-1 β. Therefore, instant specification is only enabling for the peptide of SEQ ID NO:1 having the specific inhibitory effects recited in claim 3, and not "all" possible IL-2 derived synthetic peptides having inhibitory effects on of "all" of the processes recited in claim 2. With respect to claims 4 and 7, Applicants have not demonstrated that modifying the peptide of SEQ ID NO:1, by replacing, deleting, or adding one or more natural or non-natural amino acids would not alter the activity of the peptide of SEQ ID NO:1, neither have they shown that elongating peptide of SEQ ID NO:1 by up to 4 amino acid residues at the C and/or N terminal ends would not change the specific properties of the peptide of SEQ ID NO:1. Applicants contemplate that all possible peptide fragments derived from IL-2 would have anti-inflammatory

activity and would inhibit at least one the in vitro processes recited in claim, however, Applicants fail to demonstrate that all of said peptides have the desired activities shown for the peptide of SEQ ID NO:1. Applicants have shown that a reverse sequence of pep2 (SEQ ID NO:1) does not display the same activities as the peptide of SEQ ID NO:1, however, Applicants have not shown what modifications would be tolerated by the peptide of SEQ ID NO:1, without altering the biological characteristics of said peptide. Furthermore, the state of the art is such that it is unpredictable the "all" possible fragments of IL-2 would have the desired activities. Applicants have shown that specific fragments of IL-2 have anti-inhibitory effect on some IL-2 induced processes, however, one of ordinary skill in the art would not extrapolate this the "all" possible fragments would also have all the desired activities. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant application, it will be undue experimentation to make all possible IL-2 derived synthetic peptides and test them in all of the processes recited in claim 2. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring peptide of SEQ ID NO:1, which are required for

functional and structural integrity of the peptide. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation. With respect to claim 4, Applicants have not delineated which residues of the peptide of SEQ ID NO:1 residues to be replaced or deleted, or where additions should me made, without affecting the functional integrity of the peptide of SEQ ID NO:1. Furthermore, there is no upper limit to the amount of replacements, deletions or additions. With respect to claim 11, it would be undue experimentation for skilled artisan to test fragments of IL-2 obtained from digestion with proteolytic enzymes, for in vitro ability to inhibit the adhesion of T cells with "all" possible ECM proteins, or chemotactic migration through "all" possible ECM proteins to "all" possible cytokine induced T cell proliferation or "all" possible cytokine secretion by cytokine. Instant specification discloses that enzymatic digestion of IL-2 with proteolytic enzymes results in specific fragments that display inhibitory effects on IL-2 induced adhesion of T cells to fibronectin, collagen IV or laminin, inhibited T cell chemotactic migration induced by IL-2 or MIP-1β, and inhibited spontaneous or TNF-α induced IL-8 or IL-1 β, therefore, only testing the fraction of IL-2 with these specific assays is enabled by instant disclosure.

Furthermore, the amount of embodiments corresponding to the desirable peptides, may be innumerable, and the enabled embodiments amount to only the peptide of amino acid sequence set forth in SEQ ID NO:1, said peptide having specific biological activities as recited in claim 2. Given the knowledge in the art regarding the unpredictable nature of getting biologically active peptides, as well as a lack of guidance and working examples in the specification, the skilled artisan would

not have a reasonable expectation of success that "all" possible peptides derived from IL-2 would have the desired biological activity.

With respect to claim 18, which recite "a method for treatment.....by administering an effective amount of anti-inflammatory synthetic peptide... ", what is claimed is a method of treating pancreatitis by administering "all" possible anti-inflammatory peptides, however, the instant specification demonstrates that the only enabled peptide (SEQ ID NO:1) of the instant invention has at least one of the properties recited in claim 2, and that said peptide may have therapeutic activities. Therefore, the specification is only enabling for a method of treatment by administering the peptide of SEQ ID NO:1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4, 7-8, 11-12, 14 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 1 is indefinite because it is unclear if the claim is drawn to a synthetic anti-inflammatory peptide derived from IL-2, plus anti-inflammatory derivatives of said peptide, and if so, how are these derivatives derived? How are the "Anti-inflammatory derivatives of said peptide", derived from the synthetic peptide? Does this include all or some portions of the synthetic peptide, if so which portions? Appropriate correction is required.

5b. Claim 4 recites "..... any one of claim 1....", which is improper and renders the claim indefinite. The claim should recite "The synthetic peptide of claim 1.....".

5c. Claim 4 recites "peptides obtained by deletion,.... addition or replacement of one or more amino acid residues.....', which renders the claim indefinite, because, there is no upper limit for how many amino acids to delete, replace or add. Thus, the metes and bounds of the claim can not be ascertained. Appropriate correction is required.

5d. Claim 4 (vii) is vague and indefinite, because is unclear what the dual peptides consist of, what are different peptides that are supposed to be part of this dual peptides. Appropriate correction is required. Claim 4 (viii) is also vague and indefinite, because the claim does not set the number of different or same peptides or which peptides should the multimers comprise.

5e. Claim 7 (a), is drawn to elongating the peptide of SEQ ID NO:1 by up to 4 amino acids at the C and/or N terminal ends, however, it is unclear whether the peptide should be either elongated at the C terminal, or at the end terminal or both. In other words, should 4 amino acids be added at the C terminus and 4 amino acids be added at the N terminus?

5f. Claims 4, 7 and 8 recite the acronym (pep2), which renders the claim unclear, because more than one protein can be known for the same acronym. Furthermore, there is no antecedent base for pep2. Applicant is advised to recite the full name of the protein corresponding to this acronym to obviate this rejection.

5g. Regarding claim 11, the phrase "e.g" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 8, 12 and 14 are rejected as being vague and indefinite insofar as they depend on claims 7 and 11.

Claim rejections-35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless -**
>
> ***(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.***

6. Claims 1 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Ivanov et al (WO 95/00538) published 05 January 1995.

Ivanov et al disclose anti-inflammatory peptides derived from IL-2 and a method of treating inflammatory disorders by administering said peptides, (see abstract and page 10, lines 5-29).

Instant claim 1 is drawn to an anti-inflammatory peptide derived from IL-2 and claim 18 is drawn to a method of treating inflammatory disorders by administering said anti-inflammatory peptide. Therefore, Ivanov et al reference clearly anticipates instant claims 1 and 18 in the absence of any evidence to the contrary.

Conclusion

7. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursdays from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
09 January 2003

PREMA MERTZ
PRIMARY EXAMINER